claim 43. Specifically, claim 43 has been amended to depend on claim 42 rather than claim 44. The amendments have been made without introducing new matter and no estoppels are intended thereby.

II. Claim Rejections Under 35 U.S.C. §112, First Paragraph

A. Claim 41

The Examiner has rejected claim 41 under 35 U.S.C. §112, first paragraph, as containing new subject matter. Specifically, the Examiner alleges that the proviso at the end of the definition of Y in claim 41 excludes certain pyrimidinyl compounds, which have no support in the specification. Applicants respectfully submit that this rejection has been rendered moot in view of the amendment in claim 41 that removed the proviso at the end of the definition of Y. As such, Applicants respectfully request that this rejection of claim 41 under 35 U.S.C. §112, first paragraph, be withdrawn.

B. Claims 41-51, and 53-63

The Examiner has rejected claims 41-51, and 53-63 under 35 U.S.C. §112, first paragraph, as allegedly not reasonably providing enablement for the preparation and use of compounds other than those having substituents R^5 (or R^6) as a quinolinyl ring while R^7 and R^8 are hydrogen-i.e., compound 26-6. See Office Action pages 2-3. To support this allegation, the Examiner contends that incorporating other substituents as defined by R^5–R^8 would require different starting materials and might require a different mechanism of action. Id. at 3. Additionally, the Examiner indicates that the specification does not even provide guidance for making the intermediate, 5-7, as disclosed in the general synthesis for compound 26-6. Id. The Examiner asserts that undue experimentation would be necessary to make compounds with one of R^5–R^8 as anything other than a quinolinyl ring. Id. at 4. Lastly, the Examiner takes the position that there is insufficient evidence to conclude that other compounds would share the same activity as compound 26-6. Id.

Applicants respectfully traverse this rejection. Applicants assert that the specification does enable the claims and provides ample guidance as to how to prepare compounds having various substituents defined by R^5–R^8.

In order to make a rejection based upon lack of enablement, *the Examiner has the initial burden* to establish a reasonable basis to question the enablement provided for the claimed invention. MPEP §2164.04. "A specification disclosure which contains a teaching... must be taken as being in compliance with the enablement requirement of 35 U.S.C. 112, first paragraph,

unless there is a reason to doubt the objective truth of the statements contained therein which must be relied on for enabling support." Id., emphasis added. In the present application, the Examiner has not met the initial burden of establishing a reasonable basis to question the enablement provided in the specification based on the evidence as a whole by not considering the entire scope of the disclosure including the examples and cited references.

Applicants submit that even assuming *arguendo* that the Examiner's initial burden was met, the present specification fully satisfies the enablement requirement of 35 U.S.C. 112, first paragraph. "The test of enablement is whether one reasonably skilled in the art could make or use the invention from the disclosures in the patent coupled with information known in the art without undue experimentation." *United States v. Telectronics, Inc.*, 857 F.2d 778, 785 and MPEP §2164.01. Regarding the actual disclosure of a patent, it need not teach, and preferably omits, what is well known in the art. *In re Buchner*, 929 F.2d 660, 661. Factors to be considered in the determination of an enabling disclosure have been summarized in MPEP §2164.01(a) and by the Examiner. See Office Action, page 3. Additionally, MPEP §2164.01(a) indicates that an Examiner's analysis must consider all the evidence related to each factor, and any conclusion of non-enablement must be based on the evidence as a whole.

While the specification explicitly exemplifies one compound having a pyrimidinyl group as the X substituent and a quinolinyl group as the R^5 substituent, the Examiner's assertion that undue experimentation is needed to make other compounds with other R^5-R^8 substiutents is unfounded. Applicants have provided sufficient direction and guidance to one skilled in the art wishing to make the compounds of the present invention, and have included 115 pages of extensive experimental direction that includes over 85 working examples. Included in the examples are various intermediates, such as 5-7. See Scheme 5, page 76 of the Specification. Additionally, use of a protecting group, BOC, is disclosed. See for example, Scheme 10, page 95 of the Specification. Representative examples of the R^5-R^8 substituents exemplified include: pyridinyl (specification, p. 68), benzenesulfonylamino (p.73), thienylsulfonylamino (75), quinolinyl (p. 76), 2,3,dihydro-benzofuranyl (p.83), 2-oxo-2,3-dihydro-benzoazolyl (p. 87), 3-fluorophenyl (p.92), amino (p. 107), methybenzyl (p. 121), N-oxo-quinolynyl (p. 143), aminopyridinyl (p.155), phenyl (p.159), benzothiazolyl (p.159), 4-iodo-phenylsulfonylamino (p.170), cyclohexylmethanesulfonylamino (p. 176), 7,7-dimethyl-2-oxo-bicyclo[2.2-1]hept-1(s)-ylmethanesulnylamino (p. 176), phenylmethansesulfonylamino (p. 176), cyclohezanesulfonylamino (p. 176), phenylacetylamino (p. 177), and benzyloxycarbonylamino (p. 177), benzoylamino (p. 177).

Additionally, the specification also reveals that the same R^5-R^8 substituents can be incorporated into compounds having various X substituents. See for example when R^5 is 2,3-dihydro-benzofuranyl and X is 5,6,7,8-tetrahydro-[1,8]naphthyridinyl, (compound 6-7), or X is 6,7,8,9-tetrahydro-benzo[*b*]-[1,8]naphthyridinyl, (compound 14-6). Also see for example, when R^5 is quinolinyl and X is 5,6,7,8-tetrahydro-[1,8]naphthyridinyl, (compound 15-7), or X is 1,2,3,4,6,7,8,9-octahydro-benzo[*b*]-[1,8]naphthyridinyl, (compound 21, p. 179), or X is aminopyrimidinyl, (compound 26-6).

The specification also incorporates by reference at least eight documents disclosing various synthesis techniques that can be employed to make the compounds of the present invention. See Specification, p. 66. Based upon the guidance found in the specification coupled with commonly known synthetic organic chemistry techniques, undue experimentation is not necessary to arrive at the compounds of the present invention, because it is well within the purview of the skilled artisan to synthesize various combinations of substituent additions by analogy.

As another indication of undue experimentation, the Examiner contends that there is nothing in the specification to correlate the activity of compound 26-6 with the range of the presently claim compounds in light of the unpredictable nature of the art. Specification, p. 4. The amount of guidance or direction needed to enable the invention is inversely related to the amount of knowledge in the state of the art as well as the predictability in the art. See MPEP §2164.03. However, "even in unpredictable arts, a disclosure of every operable species is not required." Id. MPEP §2164.02 specifically reveals that all actual embodiments need not be described in an application for a disclosure to be enabling. As was previously pointed out, the present specification discloses numerous species that fall within a general scope of compounds having various X substituents. A pyrimidinyl group is just one of the species disclosed. A skilled artisan armed with general knowledge of synthetic organic chemistry, could readily synthesize the claimed compounds because the present specification provides ample guidance for making numerous compounds and refers the artisan to other useful synthesis technique references. As such, the skilled artisan can make and use the presently claimed compounds without undue experimentation.

The Examiner has not made a prima facie case of non-enablement, and in light of the arguments presented, it is not reasonable to conclude that Applicants have not enabled the claims. Accordingly, Applicants respectfully request the rejection of claims 41-51, and 53-63 under 35 U.S.C. §112, first paragraph be withdrawn.

III. Claim Rejections Under 35 U.S.C. §112, Second Paragraph

The Examiner has rejected claims 43-51 under 35 U.S.C. §112, second paragraph, as allegedly indefinite for failing to particularly point out and distinctly claim the subject matter of the invention. Applicants respectfully submit that this rejection has been rendered moot in view of the amendment to correct an obvious typographical error to claim 43. Specifically, claim 43 was amended to make claim 43 depended upon claim 42 rather than claim 44. Accordingly, Applicants respectfully request that this rejection of claim 41 under 35 U.S.C. §112, second paragraph, be withdrawn.

IV. Rejection of Claims 41-51 and 53-63 under Obviousness-Type Double Patenting

Claims 41-51 and 53-63 stand provisionally rejected by the Examiner under the judicially created doctrine of obviousness-type double patenting as allegedly unpatenable over claims 1-6, and 9-16 of Application No. 09/767,471. Applicants respectfully request that this obviousness-type double patenting rejection be held in abeyance until the indication of allowable subject matter in this application, at which time, Applicants will consider the filing of a Terminal Disclaimer if still necessary to obtain allowance.

V. Requirement for Submission of Substituted Oath

The Examiner has required that a substituted oath referring to both the application and the preliminary amendment be filed in order to have the preliminary amendment be considered as part of the original disclosure. See Office Action, page 2. As basis of this requirement the Examiner references MPEP§608.04(b). Id. MPEP§608.04(b) requires that a Supplemental Oath or Declaration be filed if new matter has been introduced into the application via any amendments that were made.

Applicants respectfully submit that a Supplemental Oath is not required to be filed in the present application because a copy of the Oath or Declaration from the prior application was submitted to the Office at the same time the present divisional application and preliminary amendment was filed on July 27, 2001. This was done to rely on the earlier filed Oath or Declaration in the parent application, 09/453,847, as is outlined in MPEP§201.06(a). A copy of the transmittal letter indicating the filing of the original Oath or Declaration is attached in Appendix B. As no new matter was introduced in the Preliminary Amendment, Applicants submit that a Supplemental Oath or Declaration is not required. Accordingly, Applicants respectfully request that the filing requirement of a Supplemental Oath or Declaration be withdrawn.

VI. Allowable Subject Matter

Applicants thank the Examiner for her indications that claim 52 would be allowable if rewritten in independent form.

VII. Acknowledgment of References

Applicants acknowledge and thank the Examiner for initialing and considering the references cited in the Information Disclosure Statement filed on September 25, 2001.

In view of the foregoing remarks, Applicants respectfully request the reconsideration of the pending claims and the reexamination of the application. The timely allowance of the pending claims is respectfully requested.

If a telephonic communication with the Applicants' representative will advance the prosecution of the instant application, please telephone the representative indicated below. Applicants believe no additional fees are due but the Commissioner is authorized to charge any fees required in connection with this response to Merck Deposit Account No. 13-2755.

Respectfully submitted,

By Patricia A. Shatynski

Patricia A. Shatynski
Reg. No. 43,109
Attorney for Applicants
MERCK & CO., INC.
P.O. Box 2000
Rahway, New Jersey 07065-0907
(732) 594-1652

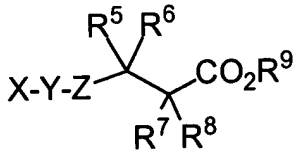
Date: May 14, 2003

Attachments: Appendix A
Appendix B

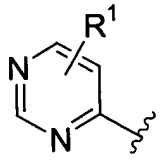
APPENDIX A

VERSION OF AMENDED CLAIMS WITH MARKINGS TO SHOW CHANGES MADE

41. (Amended) A compound of the formula



wherein X is

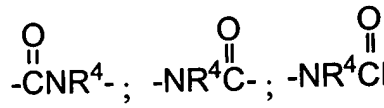


Y is selected from the group consisting of

$-(CH_2)_m-$,
$-(CH_2)_m-O-(CH_2)_n-$,
$-(CH_2)_m-NR^4-(CH_2)_n-$,
$-(CH_2)_m-S-(CH_2)_n-$,
$-(CH_2)_m-SO-(CH_2)_n-$,
$-(CH_2)_m-SO_2-(CH_2)_n-$,
$-(CH_2)_m-O-(CH_2)_n-O-(CH_2)_p-$,
$-(CH_2)_m-O-(CH_2)_n-NR^4-(CH_2)_p-$,
$-(CH_2)_m-NR^4-(CH_2)_n-NR^4-(CH_2)_p-$,
$-(CH_2)_m-O-(CH_2)_n-S-(CH_2)_p-$,
$-(CH_2)_m-S-(CH_2)_n-S-(CH_2)_p-$,
$-(CH_2)_m-NR^4-(CH_2)_n-S-(CH_2)_p-$,
$-(CH_2)_m-NR^4-(CH_2)_n-O-(CH_2)_p-$,
$-(CH_2)_m-S-(CH_2)_n-O-(CH_2)_p-$, and
$-(CH_2)_m-S-(CH_2)_n-NR^4-(CH_2)_p-$,

wherein any methylene (CH_2) carbon atom in Y, other than in R^4, can be substituted by one or two R^3 substituents[,with the proviso that when Y is $-(CH_2)_m-NR^4-(CH_2)_n-$ and n = 1, then the R^3 substituent on the methylene carbon in $-(CH_2)_m-$ adjacent to the nitrogen cannot be oxo];

Z is selected from the group consisting of



$-CH_2CH_2-$, and -CH=CH-, wherein either carbon atom can be substituted by one or two R^3 substituents;

R^1 and R^2 are each independently selected from the group consisting of

hydrogen, halogen, C_{1-10} alkyl, C_{3-8} cycloalkyl,
C_{3-8} cycloheteroalkyl, C_{3-8} cycloalkyl C_{1-6} alkyl,
C_{3-8} cycloheteroalkyl C_{1-6} alkyl, aryl, aryl C_{1-8} alkyl, amino,
amino C_{1-8} alkyl, C_{1-3} acylamino, C_{1-3} acylamino C_{1-8} alkyl,
$(C_{1-6}$ alkyl)$_p$amino, $(C_{1-6}$ alkyl)$_p$amino C_{1-8} alkyl,
C_{1-4} alkoxy, C_{1-4} alkoxy C_{1-6} alkyl, hydroxycarbonyl,
hydroxycarbonyl C_{1-6} alkyl, C_{1-3} alkoxycarbonyl,
C_{1-3} alkoxycarbonyl C_{1-6} alkyl, hydroxycarbonyl-
C_{1-6} alkyloxy, hydroxy, hydroxy C_{1-6} alkyl, C_{1-6} alkyloxy-
C_{1-6} alkyl, nitro, cyano, trifluoromethyl, trifluoromethoxy,
trifluoroethoxy, C_{1-8} alkyl-S(O)$_p$, $(C_{1-8}$alkyl)$_p$aminocarbonyl,
C_{1-8} alkyloxycarbonylamino, $(C_{1-8}$ alkyl)$_p$aminocarbonyloxy,
(aryl C_{1-8} alkyl)$_p$amino, (aryl)$_p$amino, aryl C_{1-8}
alkylsulfonylamino, and C_{1-8} alkylsulfonylamino;
or two R^1 substituents, when on the same carbon atom, are taken together with the carbon atom to which they are attached to form a carbonyl group;

each R^3 is independently selected from the group consisting of

hydrogen,
aryl,

C_{1-10} alkyl,
aryl-$(CH_2)_r$-O-$(CH_2)_s$-,
aryl-$(CH_2)_r S(O)_p$-$(CH_2)_s$-,
aryl-$(CH_2)_r$-C(O)-$(CH_2)_s$-,
aryl-$(CH_2)_r$-C(O)-N(R^4)-$(CH_2)_s$-,
aryl-$(CH_2)_r$-N(R^4)-C(O)-$(CH_2)_s$-,
aryl-$(CH_2)_r$-N(R^4)-$(CH_2)_s$-,
halogen,
hydroxyl,
oxo,
trifluoromethyl,
C_{1-8} alkylcarbonylamino,
aryl C_{1-5} alkoxy,
C_{1-5} alkoxycarbonyl,
(C_{1-8} alkyl)$_p$aminocarbonyl,
C_{1-6} alkylcarbonyloxy,
C_{3-8} cycloalkyl,
(C_{1-6} alkyl)$_p$amino,
amino C_{1-6} alkyl,
arylaminocarbonyl,
aryl C_{1-5} alkylaminocarbonyl,
aminocarbonyl,
aminocarbonyl C_{1-6} alkyl,
hydroxycarbonyl,
hydroxycarbonyl C_{1-6} alkyl,
HC≡C-$(CH_2)_t$-,
C_{1-6} alkyl-C≡C-$(CH_2)_t$-,
C_{3-7} cycloalkyl-C≡C-$(CH_2)_t$-,
aryl-C≡C-$(CH_2)_t$-,
C_{1-6} alkylaryl-C≡C-$(CH_2)_t$-,
CH_2=CH-$(CH_2)_t$-,
C_{1-6} alkyl-CH=CH-$(CH_2)_t$-,
C_{3-7} cycloalkyl-CH=CH-$(CH_2)_t$-,
aryl-CH=CH-$(CH_2)_t$-,

C_{1-6} alkylaryl-CH=CH-$(CH_2)t$-,
C_{1-6} alkyl-SO_2-$(CH_2)t$-,
C_{1-6} alkylaryl-SO_2-$(CH_2)t$-,
C_{1-6} alkoxy,
aryl C_{1-6} alkoxy,
aryl C_{1-6} alkyl,
$(C_{1-6}$ alkyl$)_p$amino C_{1-6} alkyl,
$(aryl)_p$amino,
$(aryl)_p$amino C_{1-6} alkyl,
$(aryl\ C_{1-6}$ alkyl$)_p$amino,
$(aryl\ C_{1-6}$ alkyl$)_p$amino C_{1-6} alkyl,
arylcarbonyloxy,
aryl C_{1-6} alkylcarbonyloxy,
$(C_{1-6}$ alkyl$)_p$aminocarbonyloxy,
C_{1-8} alkylsulfonylamino,
arylsulfonylamino,
C_{1-8} alkylsulfonylamino C_{1-6} alkyl,
arylsulfonylamino C_{1-6} alkyl,
aryl C_{1-6} alkylsulfonylamino,
aryl C_{1-6} alkylsulfonylamino C_{1-6} alkyl,
C_{1-8} alkoxycarbonylamino,
C_{1-8} alkoxycarbonylamino C_{1-8} alkyl,
aryloxycarbonylamino C_{1-8} alkyl,
aryl C_{1-8} alkoxycarbonylamino,
aryl C_{1-8} alkoxycarbonylamino C_{1-8} alkyl,
C_{1-8} alkylcarbonylamino,
C_{1-8} alkylcarbonylamino C_{1-6} alkyl,
arylcarbonylamino C_{1-6} alkyl,
aryl C_{1-6} alkylcarbonylamino,
aryl C_{1-6} alkylcarbonylamino C_{1-6} alkyl,
aminocarbonylamino C_{1-6} alkyl,
$(C_{1-8}$ alkyl$)_p$aminocarbonylamino,
$(C_{1-8}$ alkyl$)_p$aminocarbonylamino C_{1-6} alkyl,
$(aryl)_p$aminocarbonylamino C_{1-6} alkyl,

(aryl C_{1-8} alkyl)$_p$aminocarbonylamino,
(aryl C_{1-8} alkyl)$_p$aminocarbonylamino C_{1-6} alkyl,
aminosulfonylamino C_{1-6} alkyl,
(C_{1-8} alkyl)$_p$aminosulfonylamino,
(C_{1-8} alkyl)$_p$aminosulfonylamino C_{1-6} alkyl,
(aryl)$_p$aminosulfonylamino C_{1-6} alkyl,
(aryl C_{1-8} alkyl)$_p$aminosulfonylamino,
(aryl C_{1-8} alkyl)$_p$aminosulfonylamino C_{1-6} alkyl,
C_{1-6} alkylsulfonyl,
C_{1-6} alkylsulfonyl C_{1-6} alkyl,
arylsulfonyl C_{1-6} alkyl,
aryl C_{1-6} alkylsulfonyl,
aryl C_{1-6} alkylsulfonyl C_{1-6} alkyl,
C_{1-6} alkylcarbonyl,
C_{1-6} alkylcarbonyl C_{1-6} alkyl,
arylcarbonyl C_{1-6} alkyl,
aryl C_{1-6} alkylcarbonyl,
aryl C_{1-6} alkylcarbonyl C_{1-6} alkyl,
C_{1-6} alkylthiocarbonylamino,
C_{1-6} alkylthiocarbonylamino C_{1-6} alkyl,
arylthiocarbonylamino C_{1-6} alkyl,
aryl C_{1-6} alkylthiocarbonylamino,
aryl C_{1-6} alkylthiocarbonylamino C_{1-6} alkyl,
(C_{1-8} alkyl)$_p$aminocarbonyl C_{1-6} alkyl,
(aryl)$_p$aminocarbonyl C_{1-6} alkyl,
(aryl C_{1-8} alkyl)$_p$aminocarbonyl, and
(aryl C_{1-8} alkyl)$_p$aminocarbonyl C_{1-6} alkyl;
or two R^3 substituents, when on the same carbon atom are taken together with the carbon atom to which they are attached to form a carbonyl group or a cyclopropyl group,

wherein any of the alkyl groups of R^3 are either unsubstituted or substituted with one to three R^1 substituents, and provided that each R^3 is selected such that in the resultant compound the carbon atom or atoms to which R^3 is attached is itself attached to no more than one heteroatom;

each R^4 is independently selected from the group consisting of

hydrogen,
aryl,
aminocarbonyl,
C_{3-8} cycloalkyl,
amino C_{1-6} alkyl,
$(aryl)_p$aminocarbonyl,
$(aryl\ C_{1-5}\ alkyl)_p$aminocarbonyl,
hydroxycarbonyl C_{1-6} alkyl,
C_{1-8} alkyl,
aryl C_{1-6} alkyl,
$(C_{1-6}\ alkyl)_p$amino C_{2-6} alkyl,
$(aryl\ C_{1-6}\ alkyl)_p$amino C_{2-6} alkyl,
C_{1-8} alkylsulfonyl,
C_{1-8} alkoxycarbonyl,
aryloxycarbonyl,
aryl C_{1-8} alkoxycarbonyl,
C_{1-8} alkylcarbonyl,
arylcarbonyl,
aryl C_{1-6} alkylcarbonyl,
$(C_{1-8}\ alkyl)_p$aminocarbonyl,
aminosulfonyl,
C_{1-8} alkylaminosulfonyl,
$(aryl)_p$aminosulfonyl,
$(aryl\ C_{1-8}\ alkyl)_p$aminosulfonyl,
arylsulfonyl,
arylC1-6 alkylsulfonyl,
C_{1-6} alkylthiocarbonyl,
arylthiocarbonyl, and
aryl C_{1-6} alkylthiocarbonyl,

wherein any of the alkyl groups of R^4 are either unsubstituted or substituted with one to three R^1 substituents;

R^5 and R^6 are each independently selected from the group consisting of

hydrogen,

C_{1-10} alkyl,
aryl,
aryl-$(CH_2)_r$-O-$(CH_2)_s$-,
aryl-$(CH_2)_r S(O)_p$-$(CH_2)_s$-,
aryl-$(CH_2)_r$-C(O)-$(CH_2)_s$-,
aryl-$(CH_2)_r$-C(O)-N(R^4)-$(CH_2)_s$-,
aryl-$(CH_2)_r$-N(R^4)-C(O)-$(CH_2)_s$-,
aryl-$(CH_2)_r$-N(R^4)-$(CH_2)_s$-,
halogen,
hydroxyl,
C_{1-8} alkylcarbonylamino,
aryl C_{1-5} alkoxy,
C_{1-5} alkoxycarbonyl,
(C_{1-8} alkyl)$_p$aminocarbonyl,
C_{1-6} alkylcarbonyloxy,
C_{3-8} cycloalkyl,
(C_{1-6} alkyl)$_p$amino,
amino C_{1-6} alkyl,
arylaminocarbonyl,
aryl C_{1-5} alkylaminocarbonyl,
aminocarbonyl,
aminocarbonyl C_{1-6} alkyl,
hydroxycarbonyl,
hydroxycarbonyl C_{1-6} alkyl,
HC≡C-$(CH_2)_t$-,
C_{1-6} alkyl-C≡C-$(CH_2)_t$-,
C_{3-7} cycloalkyl-C≡C-$(CH_2)_t$-,
aryl-C≡C-$(CH_2)_t$-,
C_{1-6} alkylaryl-C≡C-$(CH_2)_t$-,
CH_2=CH-$(CH_2)_t$-,
C_{1-6} alkyl-CH=CH-$(CH_2)_t$-,
C_{3-7} cycloalkyl-CH=CH-$(CH_2)_t$-,
aryl-CH=CH-$(CH_2)_t$-,
C_{1-6} alkylaryl-CH=CH-$(CH_2)_t$-,

C_{1-6} alkyl-SO_2-$(CH_2)t$-,
C_{1-6} alkylaryl-SO_2-$(CH_2)t$-,
C_{1-6} alkoxy,
aryl C_{1-6} alkoxy,
aryl C_{1-6} alkyl,
$(C_{1-6}$ alkyl$)_p$amino C_{1-6} alkyl,
$(aryl)_p$amino,
$(aryl)_p$amino C_{1-6} alkyl,
(aryl C_{1-6} alkyl$)_p$amino,
(aryl C_{1-6} alkyl$)_p$amino C_{1-6} alkyl,
arylcarbonyloxy,
aryl C_{1-6} alkylcarbonyloxy,
$(C_{1-6}$ alkyl$)_p$aminocarbonyloxy,
C_{1-8} alkylsulfonylamino,
arylsulfonylamino,
C_{1-8} alkylsulfonylamino C_{1-6} alkyl,
arylsulfonylamino C_{1-6} alkyl,
aryl C_{1-6} alkylsulfonylamino,
aryl C_{1-6} alkylsulfonylamino C_{1-6} alkyl,
C_{1-8} alkoxycarbonylamino,
C_{1-8} alkoxycarbonylamino C_{1-8} alkyl,
aryloxycarbonylamino C_{1-8} alkyl,
aryl C_{1-8} alkoxycarbonylamino,
aryl C_{1-8} alkoxycarbonylamino C_{1-8} alkyl,
C_{1-8} alkylcarbonylamino,
C_{1-8} alkylcarbonylamino C_{1-6} alkyl,
arylcarbonylamino C_{1-6} alkyl,
aryl C_{1-6} alkylcarbonylamino,
aryl C_{1-6} alkylcarbonylamino C_{1-6} alkyl,
aminocarbonylamino C_{1-6} alkyl,
$(C_{1-8}$ alkyl$)_p$aminocarbonylamino,
$(C_{1-8}$ alkyl$)_p$aminocarbonylamino C_{1-6} alkyl,
$(aryl)_p$aminocarbonylamino C_{1-6} alkyl,
(aryl C_{1-8} alkyl$)_p$aminocarbonylamino,

(aryl C_{1-8} alkyl)$_p$aminocarbonylamino C_{1-6} alkyl,
aminosulfonylamino C_{1-6} alkyl,
(C_{1-8} alkyl)$_p$aminosulfonylamino,
(C_{1-8} alkyl)$_p$aminosulfonylamino C_{1-6} alkyl,
(aryl)$_p$aminosulfonylamino C_{1-6} alkyl,
(aryl C_{1-8} alkyl)$_p$aminosulfonylamino,
(aryl C_{1-8} alkyl)$_p$aminosulfonylamino C_{1-6} alkyl,
C_{1-6} alkylsulfonyl,
C_{1-6} alkylsulfonyl C_{1-6} alkyl,
arylsulfonyl C_{1-6} alkyl,
aryl C_{1-6} alkylsulfonyl,
aryl C_{1-6} alkylsulfonyl C_{1-6} alkyl,
C_{1-6} alkylcarbonyl,
C_{1-6} alkylcarbonyl C_{1-6} alkyl,
arylcarbonyl C_{1-6} alkyl,
aryl C_{1-6} alkylcarbonyl,
aryl C_{1-6} alkylcarbonyl C_{1-6} alkyl,
C_{1-6} alkylthiocarbonylamino,
C_{1-6} alkylthiocarbonylamino C_{1-6} alkyl,
arylthiocarbonylamino C_{1-6} alkyl,
aryl C_{1-6} alkylthiocarbonylamino,
aryl C_{1-6} alkylthiocarbonylamino C_{1-6} alkyl,
(C_{1-8} alkyl)$_p$aminocarbonyl C_{1-6} alkyl,
(aryl)$_p$aminocarbonyl C_{1-6} alkyl,
(aryl C_{1-8} alkyl)$_p$aminocarbonyl, and
(aryl C_{1-8} alkyl)$_p$aminocarbonyl C_{1-6} alkyl;

or R^5 and R^6 are taken together with the carbon atom to which they are attached to form a carbonyl group,

wherein any of the alkyl groups of R^5 or R^6 are either unsubstituted or substituted with one to three R^1 substituents, and provided that each R^5 and R^6 are selected such that in the resultant compound the carbon atom to which R^5 and R^6 are attached is itself attached to no more than one heteroatom;

R^7 and R^8 are each independently selected from the group consisting of

hydrogen,
C_{1-10} alkyl,
aryl,
aryl-$(CH_2)_r$-O-$(CH_2)_s$-,
aryl-$(CH_2)_r S(O)_p$-$(CH_2)_s$-,
aryl-$(CH_2)_r$-C(O)-$(CH_2)_s$-,
aryl-$(CH_2)_r$-C(O)-N(R^4)-$(CH_2)_s$-,
aryl-$(CH_2)_r$-N(R^4)-C(O)-$(CH_2)_s$-,
aryl-$(CH_2)_r$-N(R^4)-$(CH_2)_s$-,
halogen,
hydroxyl,
C_{1-8} alkylcarbonylamino,
aryl C_{1-5} alkoxy,
C_{1-5} alkoxycarbonyl,
(C_{1-8} alkyl)$_p$aminocarbonyl,
C_{1-6} alkylcarbonyloxy,
C_{3-8} cycloalkyl,
(C_{1-6} alkyl)$_p$amino,
amino C_{1-6} alkyl,
arylaminocarbonyl,
aryl C_{1-5} alkylaminocarbonyl,
aminocarbonyl,
aminocarbonyl C_{1-6} alkyl,
hydroxycarbonyl,
hydroxycarbonyl C_{1-6} alkyl,
HC≡C-$(CH_2)_t$-,
C_{1-6} alkyl-C≡C-$(CH_2)_t$-,
C_{3-7} cycloalkyl-C≡C-$(CH_2)_t$-,
aryl-C≡C-$(CH_2)_t$-,
C_{1-6} alkylaryl-C≡C-$(CH_2)_t$-,
CH_2=CH-$(CH_2)_t$-,
C_{1-6} alkyl-CH=CH-$(CH_2)_t$-,
C_{3-7} cycloalkyl-CH=CH-$(CH_2)_t$-,
aryl-CH=CH-$(CH_2)_t$-,

C_{1-6} alkylaryl-CH=CH-$(CH_2)t$-,
C_{1-6} alkyl-SO_2-$(CH_2)t$-,
C_{1-6} alkylaryl-SO_2-$(CH_2)t$-,
C_{1-6} alkoxy,
aryl C_{1-6} alkoxy,
aryl C_{1-6} alkyl,
$(C_{1-6}$ alkyl$)_p$amino C_{1-6} alkyl,
$(aryl)_p$amino,
$(aryl)_p$amino C_{1-6} alkyl,
(aryl C_{1-6} alkyl$)_p$amino,
(aryl C_{1-6} alkyl$)_p$amino C_{1-6} alkyl,
arylcarbonyloxy,
aryl C_{1-6} alkylcarbonyloxy,
$(C_{1-6}$ alkyl$)_p$aminocarbonyloxy,
C_{1-8} alkylsulfonylamino,
arylcarbonylamino,
arylsulfonylamino,
C_{1-8} alkylsulfonylamino C_{1-6} alkyl,
arylsulfonylamino C_{1-6} alkyl,
aryl C_{1-6} alkylsulfonylamino,
aryl C_{1-6} alkylsulfonylamino C_{1-6} alkyl,
C_{1-8} alkoxycarbonylamino,
C_{1-8} alkoxycarbonylamino C_{1-8} alkyl,
aryloxycarbonylamino C_{1-8} alkyl,
aryl C_{1-8} alkoxycarbonylamino,
aryl C_{1-8} alkoxycarbonylamino C_{1-8} alkyl,
C_{1-8} alkylcarbonylamino C_{1-6} alkyl,
arylcarbonylamino C_{1-6} alkyl,
aryl C_{1-6} alkylcarbonylamino,
aryl C_{1-6} alkylcarbonylamino C_{1-6} alkyl,
aminocarbonylamino C_{1-6} alkyl,
arylaminocarbonylamino,
$(C_{1-8}$ alkyl$)_p$aminocarbonylamino,
$(C_{1-8}$ alkyl$)_p$aminocarbonylamino C_{1-6} alkyl,

(aryl)$_p$aminocarbonylamino C_{1-6} alkyl,
(aryl C_{1-8} alkyl)$_p$aminocarbonylamino,
(aryl C_{1-8} alkyl)$_p$aminocarbonylamino C_{1-6} alkyl,
aminosulfonylamino C_{1-6} alkyl,
(C_{1-8} alkyl)$_p$aminosulfonylamino,
(C_{1-8} alkyl)$_p$aminosulfonylamino C_{1-6} alkyl,
(aryl)$_p$aminosulfonylamino C_{1-6} alkyl,
(aryl C_{1-8} alkyl)$_p$aminosulfonylamino,
(aryl C_{1-8} alkyl)$_p$aminosulfonylamino C_{1-6} alkyl,
C_{1-6} alkylsulfonyl,
C_{1-6} alkylsulfonyl C_{1-6} alkyl,
arylsulfonyl C_{1-6} alkyl,
aryl C_{1-6} alkylsulfonyl,
aryl C_{1-6} alkylsulfonyl C_{1-6} alkyl,
C_{1-6} alkylcarbonyl,
C_{1-6} alkylcarbonyl C_{1-6} alkyl,
arylcarbonyl C_{1-6} alkyl,
aryl C_{1-6} alkylcarbonyl,
aryl C_{1-6} alkylcarbonyl C_{1-6} alkyl,
C_{1-6} alkylthiocarbonylamino,
C_{1-6} alkylthiocarbonylamino C_{1-6} alkyl,
arylthiocarbonylamino C_{1-6} alkyl,
aryl C_{1-6} alkylthiocarbonylamino,
aryl C_{1-6} alkylthiocarbonylamino C_{1-6} alkyl,
(C_{1-8} alkyl)$_p$aminocarbonyl C_{1-6} alkyl,
(aryl)$_p$aminocarbonyl C_{1-6} alkyl,
(aryl C_{1-8} alkyl)$_p$aminocarbonyl,
(aryl C_{1-8} alkyl)$_p$aminocarbonyl C_{1-6} alkyl, and
C_{7-20} polycyclyl C_{0-8} alkylsulfonylamino,

wherein any of the alkyl groups of $R^7$and R^8 are either unsubstituted or substituted with one to three R^1 substituents, and provided that each $R^7$and R^8 are selected such that in the resultant compound the carbon atom to which R^7 and R^8 are attached is itself attached to no more than one heteroatom;

R^9 is selected from the group consisting of

hydrogen,
C_{1-8} alkyl,
aryl,
aryl C_{1-8} alkyl,
C_{1-8} alkylcarbonyloxy C_{1-4} alkyl,
aryl C_{1-8} alkylcarbonyloxy C_{1-4} alkyl,
C_{1-8} alkylaminocarbonylmethylene, and
C_{1-8} dialkylaminocarbonylmethylene;

wherein
each m is independently an integer from 0 to 6;
each n is independently an integer from 0 to 6;
each p is independently an integer from 0 to 2;
each r is independently an integer from 1 to 3;
each s is independently an integer from 0 to 3; and
each t is independently an integer from 0 to 3;

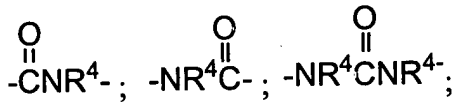
and the pharmaceutically acceptable salts thereof.

42. (Amended) The compound of Claim 41 wherein Y is selected from the group consisting of

$-(CH_2)_m-$,
$-(CH_2)_m-O-(CH_2)_n-$,
$-(CH_2)_m-NR^4-(CH_2)_n-$,
$-(CH_2)_m-S-(CH_2)_n-$,
$-(CH_2)_m-SO-(CH_2)_n-$,
$-(CH_2)_m-SO_2-(CH_2)_n-$,
$-(CH_2)_m-O-(CH_2)_n-O-(CH_2)_p-$,
$-(CH_2)_m-O-(CH_2)_n-NR^4-(CH_2)_p-$,
$-(CH_2)_m-NR^4-(CH_2)_n-NR^4-(CH_2)_p-$, and
$-(CH_2)_m-NR^4-(CH_2)_n-O-(CH_2)_p-$,

wherein any methylene (CH_2) carbon atom in Y, other than in R^4, can be substituted by one or two R^3 substituents[, with the proviso that when Y is $-(CH_2)_m-NR^4-(CH_2)_n-$ and n = 1, then the R^3 substituent on the methylene carbon in $-(CH_2)_m-$ adjacent to the nitrogen cannot be oxo];

and Z is selected from the group consisting of



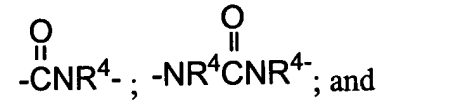
-CH2CH2-, and -CH=CH-, wherein either carbon atom can be substituted by one or two R^3 substituents.

43. (Amended) The compound of Claim [44] **42** wherein Y is selected from the group consisting of

$(CH_2)_m$, $(CH_2)_m-S-(CH_2)_n$, and $(CH_2)_m-NR^4-(CH_2)_n$,

wherein any methylene (CH_2) carbon atom in Y, other than in R^4, can be substituted by one or two R^3 substituents[, with the proviso that when Y is $-(CH_2)_m-NR^4-(CH_2)_n-$ and n = 1, then the R^3 substituent on the methylene carbon in $-(CH_2)_m-$ adjacent to the nitrogen cannot be oxo];

and Z is selected from the group consisting of



-CH2CH2-, wherein either carbon atom can be substituted by one or two R^3 substituents.

APPENDIX B

P nt Case No	20009YDB

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

MAY 19 2003 PATENT & TRADEMARK OFFICE

Assistant Commissioner for Patents
Washington, D.C. 20231

Prior Application:

Examiner	D. Rao
Art Unit	1624

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TECH CENTER 1600/2900

Sir: This is a request for filing a ☐ Continuation ☒ Divisional application, under 37 C.F.R. 1.53(b), of pending application Serial No. 09/453,847 filed on December 2, 1999 (DATE) of Askew et al. (INVENTOR)

for INTEGRIN RECEPTOR ANTAGONISTS (TITLE OF INVENTION)

1. The enclosed comprises a copy of prior application Serial No. 09/453,847, as filed on December 2, 1999. The entire disclosure of this prior application is hereby incorporated by reference.

2. The filing fee is calculated below:

CLAIMS AS FILED IN THE PRIOR APPLICATION, LESS ANY CLAIMS CANCELED BY AMENDMENT BELOW

FOR	NUMBER FILED		NUMBER EXTRA			RATE	FEE	
Total Claims	23	-	20	3	x	$18	$54	
Independent Claims	1	-	3	0	x	$80	$0	
*Multiple Dependent Claims					x	$270		
Basic Fee (minimum amount required)							$710	
* Add this fee if application contains any multiple dependent claims, regardless of number.							$764	Total Fee

3. The Assistant Commissioner is hereby authorized to charge any fees which may be required or to credit any overpayment to Account No. 13-2755.

DOCKETED
AUG 01 2001
BARBARA REIL

4. ☐ Amend the specification by inserting before the first line the sentence:
-- This is a ☐ continuation, ☐ division of application Serial No. _____, filed _____.

5. ☐ Cancel in this application original claims: _____

6. ☒ Preliminary amendment enclosed.

7. ☐ Information Disclosure Statement/PTO-1449 enclosed.

8a. ☐ Transfer the drawings from the prior application to this application and abandon said prior application as of the filing date accorded this application. A duplicate copy of this sheet is enclosed for filing in the prior application file.

8b. ☐ New formal drawings are enclosed.

9a. ☐ Priority of application Serial No. _____, filed _____, in _____ (COUNTRY) is claimed under 35 U.S.C. 119.

9b. ☐ The certified copy of the priority application has been filed in prior application Serial No. _____, filed _____.

10. ☐ The prior application is assigned to _____

11. ☐ The undersigned attorney or agent has:
a. ☒ Power in the prior application as originally filed.
b. ☐ Associate power, copy enclosed.

EXPRESS MAIL CERTIFICATE

DATE OF DEPOSIT July 27, 2001

EXPRESS MAIL NO. EL523909858US

I HEREBY CERTIFY THAT THIS CORRESPONDENCE IS BEING DEPOSITED WITH THE UNITED STATES POSTAL SERVICE AS EXPRESS MAIL "POST OFFICE TO ADDRESSEE" ON THE ABOVE DATE IN AN ENVELOPE ADDRESSED TO ASSISTANT COMMISSIONER FOR PATENTS, WASHINGTON, D.C. 20231.

MAILED BY G B Crowley DATE 7-27-01

Respectfully,

Philippe L. Durette

By: Philippe L. Durette
Attorney for Applicant(s)
Registration No. 35,125
Telephone: (732) 594-4568
Address: Merck & Co., Inc.
Patent Department
P.O. Box 2000 - RY60-30
Rahway, N.J. 07065-0907
Date: July 27, 2001

—IN DUPLICATE Enclosure